ENHANCERS OF CFTR CHLORIDE CHANNEL FUNCTION

ABSTRACT

Phosphorylation of the cystic fibrosis transmembrane conductance regulator (CFTR) by cyclic AMP-dependent protein kinase (PKA) is essential for opening the CFTR chloride channel. A short segment containing many negatively charged amino acids (817-838, NEG2) within the regulatory (R) domain of CFTR is a critical regulator of the chloride channel activity. Deletion of NEG2 from CFTR completely eliminates the PKA dependence of the chloride channel. Exogenous NEG2 peptide interacts with the CFTR molecule and exhibits stimulatory effects on CFTR function. Our data suggest that NEG2 interacts with other cytosolic domains of CFTR to control the opening transitions of the chloride channel.